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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,380	04/18/2000	Donald Choy Chang	MLY-5	2514
22827	7590	09/12/2005		
DORITY & MANNING, P.A. POST OFFICE BOX 1449 GREENVILLE, SC 29602-1449			EXAMINER FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 09/12/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/551,380

Applicant(s)

CHANG ET AL. 3

Examiner

Christian L. Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE \_\_\_\_\_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,7,25,26,28,30-34 and 36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,7,25,26,28,30 and 32-34 is/are rejected.
- 7) ☒ Claim(s) 31 and 36 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 April 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>8,10/00 5/02;5/05</u>   | 6) <input type="checkbox"/> Other: _____                                    |

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### DETAILED ACTION

1. Claims 1, 2, 7, 25, 26, 28, 30-34, and 36 are pending and under consideration in this Office Action.
2. The rejection of claims 1, 2, 25, 26, 28, 29, and 34 under 35 U.S.C. 102(b) as being anticipated by Xu et al. has been withdrawn in view of applicants amendment filed 06/22/2005.
3. Claim 31 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).
4. Claim 36 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 7. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:  
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
6. Claims 28, 30, 32, 33, and 34 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Applicants' arguments filed 06/22/2005 have been fully considered but are not persuasive. Applicants' position is that the specification disclose an adequate number of fluorescent proteins as encompassed by the claims and that these proteins have been disclosed to have specific protease recognition sites. The examiner respectfully disagrees for reasons of record as supplemented below.

In the evaluation of the claims for compliance with the written description requirement of 35 U.S.C. 112, of particular relevance is 66 FR 1099, Friday, January 5, 2001, which states: "*Eli Lilly* explains that a chemical compound's name does not necessarily convey a written description of the named chemical compound, particularly when a genus of compounds is claimed. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1405. The name, if it does no more than distinguish the claimed genus from all others by function, does not satisfy the written description requirement because "it does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Thus *Eli Lilly* identified a set of circumstances in which the words of the claim did not, without more, adequately convey to others that applicants had possession of what they claimed." (see p. 1100, 1<sup>st</sup> column, line 47 to 2<sup>nd</sup> column, line 2).

The claims are genus claims that are directed toward single genetically engineered green fluorescent proteins from any biological source of any amino acid sequence and structure having the recited loops and beta sheets comprising any protease cleavage site of any amino acid sequence and structure, wherein proteolytic cleavage at said cleavage site causes alteration of any one of emission and excitation spectra of said fluorescent proteins. The scope of the claims includes many fluorescent proteins from many biological sources, where the fluorescent proteins have widely differing structural, chemical, and physical characteristics. The claimed genus is highly variable because a significant number of structural differences between genus members exists. Furthermore, the scope of the claims is not limited to the fluorescent proteins disclosed in the specification.

The recitation of the name of the chemical compound the genus (e.g., single genetically engineered green fluorescent protein) does not define any structural features commonly possessed by each claimed genus nor define any structural features commonly possessed by each claimed

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genus. The specification does not describe and define any structural features commonly possessed by the claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of each genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the claimed a genus.

### ***Claim Rejections - 35 U.S.C. § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 28, 30, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cody et al. (Biochemistry. 1993 Feb 9;32(5):1212-8; ABSTRACT) in view of Xu et al. (Nucleic Acids Res. 1998 Apr 15;26(8):2034-5; reference of record).

Cody et al. teach the *Aequorea Victoria* green-fluorescent protein (GFP) single chromophore composed of modified amino acid residues within the polypeptide (see Abstract).

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The claims differ from the teachings of Cody et al. in that the taught GFP does not have an inserted caspase cleavage site.

The teachings of Xu et al. have been previously stated in the Office Action dated 10/24/2001. Specifically, Xu et al. teach the amino acid sequence of the caspase-3 (CPP32) cleavage site DEVD (see entire publication and Figure 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the GFP taught by Cody et al. such that the caspase-3 (CPP32) cleavage site DEVD is inserted into its loop structure.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this to provide an alternative substrate in an assay for caspase activity where destruction of fluorescence emitted by the modified GFP can be monitored. Furthermore, Xu et al. provide evidence that GFP can be expressed in cells and can be used to monitor the events of programmed cell death.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time the invention was made, and was as a whole clearly *prima facie* obvious.

### ***Conclusion***

9. Claims 1, 2, 4, 7, 25, 26 allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

CLF

  
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